statistical patterns nearly optimal for an efficient exploration of the environment. This exploratory motion is at the basis of contact formation and the establishment of appropriate synaptic connections. Filopodia and lamellipodia can also avoid obstacles and occasionally lamellipodia can displace them. From this point of view, filopodial and lamellipodial motion can be described as a random process in which errors are corrected by efficient feed-back loops. We argue that neurons not only process sensory signals, but also solve mechanical problems throughout their entire lifespan, from the early stages of embryogenesis to adulthood.

3242-Pos Board B289
Assessing the Dynamics and Mechanics of the Cell Membrane
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Thermally and actively driven cell membrane fluctuations are known to be readouts for the nanomechanical interaction between the cortical cytoskeleton and the plasma membrane and the membrane. In this study, we developed a non-contact method to measure cell surface fluctuations through measurements of resistance between a microelectrode tip and the cell membrane. The system resolution was < 2 nm tested by using 2-10 Hz sinusoidal piezo stage motion with amplitudes ranging from 2 nm to 100 nm. We found that endothelial cells exhibited local membrane fluctuations of ~20 nm at a number of characteristic frequencies. To determine the role of actin in membrane fluctuation, we treated cells with 2 μM of actin depolymerizing drug, cytochalasin D, and we found that actin depolymerization increased in fluctuation amplitude up to 2 times at all frequencies. Finally, to determine role of ATP in membrane fluctuations, we treated cells with ATP depletion drug cocktail which consisted of 25nM Antimycin A + 2mg/ml 2-Deoxy-D-Glucose, and we found that ATP depletion abolished all membrane fluctuations. Therefore, actin cytoskeleton and dynamic processes facilitated by ATP may modulate membrane functions through mechanical effects on membrane fluctuations

3243-Pos Board B290
Cell Coat Mediated Cell Migration
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Cell migration depends on a sequence of adhesion and detachment events. These events arise during the cyclic migration process, which involves the integrin-dependent adhesion machinery, the acto-myosin system and the signaling pathways between them. Migration appears to rely on a delicate spatio-temporal regulation of cell adhesion to the surrounding substrate. Studies of cell migration in physiological contexts have shown that a pericellular coat, a thickened polymer matrix attached to many cell surfaces, often is required to facilitate cell migration, including that of aggressively spreading cancers. Cell motility in these systems directly depends on the formation of a large, hyaluronan-rich cell coat with an asymmetric distribution around the polarized migrating cell. Removal or alteration of the coat substantially decreases motility - to the point that such treatments have been proposed as therapies for some types of cancer. The hyaluronan biology community often speculates that cell migration requires the 'insulation' and/or the mechanical properties provided by the cell coat. However, little has been done to substantiate this claim. A bigger problem yet is that the lubricating effect of hyaluronan has been shown to oppose adhesion, which leads to a conundrum in the present context: How is it possible that inhibition of adhesion can help a cell migrate, when adhesion is absolutely necessary to gain traction and exert the force to move the cell forward? We have developed a microfluidics-based cell migration assay capable of presenting several surface gradients of fibronectin of different slopes to induce cell migration within the same device. We study the ability of these gradients to induce cell migration and their influence on the cell coat phenotype and mechanical properties using a combination of fluorescent labeling, particle exclusion assays, and optical tweezer force probe experiments.

3244-Pos Board B291
Biophysics of Tumor Cell Adhesion: From single molecules to multi-cellular interactions
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Cell adhesion plays a critical role in tumor formation, invasion and metastasis. The complex processes underlying adhesion to other cells and the extra-cellular matrices are dynamic and inherently multi-scale. Unfortunately, computational and mathematical models aimed at understanding adhesion have traditionally focused on a single length-scale and have been unable to link events at the atomic and molecular scale to bulk behaviors seen in experiments. In addition, most adhesion models have been blind to the effects of matrix structure and mechanics, molecular sequence and conformations and hence can only make qualitative predictions. Using a combination of molecular dynamics to generate conformations, coarse-graining of these results for single-chain mean field theory and then further coarse graining too study processes at the bulk level, we have developed a fully multi-scale model of cell-matrix and cell-cell interactions. Our models are rooted in principles of thermodynamics, statistical and continuum mechanics and are able to capture cell-matrix and cell-cell adhesion events at a single molecular, cellular, multi-cellular and tissue level. We are also able to study the effects of soluble and insoluble ligands, functionalized nano-particles and tethered surfaces. Thus our model is able to make quantitative predictions in both in vivo and in vitro environments.

3245-Pos Board B292
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The free energy that drives growth, resorption and sliding of focal adhesions includes mechanical and chemical contributions. We have identified a competition among four effects that control focal adhesion dynamics: (1) work done during addition of complexes, (2) the chemical potential inherent to focal adhesions, (3) the elastic free energy associated with deformation of focal adhesions, and (4) work done on a molecular conformational change. A theoretical treatment of focal adhesion dynamics developed in the framework of rate processes driven by thermodynamics demonstrates that the mechanisms governed by these four effects allow focal adhesions to exhibit a rich variety of behavior without the need to introduce special constitutive assumptions. In this treatment, the structural unit of focal adhesions is a complex consisting of a ligand such as fibronectin, an integrin molecule, and associated plaque proteins. The binding and unbinding of these complexes causes focal adhesion growth and resorption, respectively. The reaction-limited case is considered. Our central findings are that growth, resorption and sliding are all predicted by a very simple chemo-mechanical model. Sliding requires symmetry breaking and is achieved via (1) above; (4) promotes symmetric growth, and (2) and (3) cause symmetric desorption. The role of kinetic modulation is also examined.

3246-Pos Board B293
Micromechanical Properties Of Fixed And Living Vascular Pulmonary Endothelial Cells Following Exposure To Barrier Enhancing And Barrier Disrupting Agents
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Disruption of pulmonary endothelial cell (EC) barrier function is a critical pathophysiologic event that occurs in multiple inflammatory disease processes. The actin cytoskeleton, an essential regulator of endothelial permeability, is a dynamic structure whose stimuli-induced rearrangement is linked to barrier modulation. We used atomic force microscopy (AFM) to characterize structural and mechanical changes in the F-actin cytoskeleton of cultured human pulmonary artery EC in response to both barrier-enhancing and barrier-disrupting conditions. The mechanical properties of both fixed and live cells were evaluated. Elastic modulus values in the range of 50-1000 kPa were typically measured for fixed cells, while much lower values of 1-40 kPa were characteristic of live cells. In fixed cells, a differential distribution of elasticity was observed after exposure to the barrier-enhancing compound S1P (sphingosine 1-phosphate) compared to that produced by the barrier-disrupting agonist, thrombin. After S1P, the elastic modulus was elevated primarily at the periphery, while thrombin treatment increased elasticity in the central region of the cell. These observations correspond with the distribution of F-actin in parallel-treated EC as detected by immunofluorescence. In living cells, thrombin generally increased the average elastic modulus over 60 minutes; however, the S1P response was more varied and subtle. Experiments are under way to confirm these preliminary observations. These results provide novel insights into the structural and mechanical properties that dynamically regulate pulmonary EC barrier function.

3247-Pos Board B294
Adaptive-Control Model for Neutrophil ORIENTATION in the Direction of Chemical Gradients
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Directional movement of neutrophils in spatial chemical gradients is the result of complex intracellular signaling mechanisms that are not yet fully understood. Although many of the signaling molecules that participate in the mechanisms of gradient detection in neutrophils are already known, current models still cannot provide satisfactory explanation for the initial orientation in the direction of chemical gradients. To address these challenges, we propose a new biophysical model for neutrophil orientation in the direction of chemical